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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/460,107	12/13/99	ASTLE T	130-129

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HM12/1004

EXAMINER	
LU,F	
ART UNIT	**PAPER NUMBER**
1655	5

DATE MAILED: 10/04/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/460,107	Astle
Examiner	**Group Art Unit**
Frank Lu	1655

☒ Responsive to communication(s) filed on *Jul 31, 2000*.

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-28* is/are pending in the application.

Of the above, claim(s) *1-11* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *12-28* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☒ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group II, claims 12-28 in Paper No. 4 is acknowledged. The traversal is on the ground(s) that "all claims in the application are closely related and should be examined together for reasons of efficiency and economy". The above arguments have been fully considered and have not been found pervasive toward the withdrawal of the restriction requirement nor pervasive toward the relaxation of same such that Groups I and II will be examined together. The examiner has clearly indicated in Election/Restriction of Paper No. 3 that Groups I and II are related as product and process of use. Restriction between these admittedly related groups is proper because the process for using the product as claimed can be practiced with another materially different product such as any regular PCR apparatus. Reason of efficiency and economy on the part of applicant are not dispositive of the burden placed upon the examiner. The requirement is still deemed proper and is therefore made FINAL.

2. This application contains claims 1-11 are drawn to an invention nonelected with traverse in Paper No. 4. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Priority

3. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78).

Oath/Declaration

4. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because applicant has not declared the priority of earlier applications which were shown in the specification (page 2)

Drawings

5. The drawings remain objected to for reasons as stated on FORM PTO-948 (Rev. 8-98). Applicant is required to submit a proposed drawing correction in reply to this Office action. However, formal correction of the noted defect can be deferred until the application is allowed by the examiner.

Response to Arguments

The applicant's request that "submission of formal drawings be deferred until a Notice of Allowance is issues in the application" is granted.

Specification

6. The disclosure remains objected to because of the following informalities: Both Application Serial Nos. 09/271,050 and 09/198,018 are pending application. No patent has issued for these cases. The applicant is advised to delete US Patent No. and issued date on line 4, 5, and 8 of page 2 of subject application. Please check the specification for mistakes.

Appropriate correction is required.

Response to Arguments

The argument " the missing information is still not available, but will be inserted when it does become available" have been fully considered and have not been found pervasive since no patent has issued for the cases 09/271,050 or 09/198,018. The applicant is advised to delete US Patent No. and issued date on line 4, 5, and 8 of page 2 of subject application.

Claim Rejections - 35 U.S.C. § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any

> person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 12-28 remains rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *In re Wands 858 F. 2d 731*, 8 USPQ2nd 1400 (CAFC 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'". Clearly, enablement of a claimed invention cannot be predicted on the basis of quantity of experimentation required to make or use the invention. " Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations". Enablement is considered in view of the wands factors (MPEP 2164.01(a)). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Quantity of Experimentation Necessary & The Amount of Direction or Guidance Provided

Claims 12-28 in this instant application are directed to an apparatus for performing a reagent protocol using polymerase chain reaction.

The claims have sufficient breadth of scope so to encompass an automated apparatus for performing a reagent protocol using polymerase chain reaction with any size of reagent well. The specification does not provide adequate guidance for use of any kind of well format (any size of reagent well) in an apparatus for performing a reagent protocol using polymerase chain reaction. The specification does not enable the making of the apparatus for performing a reagent protocol using polymerase chain reaction with undefined size of reagent wells.

The claims have sufficient breadth of scope so to encompass automated control means. The specification does not set forth any software by which such an apparatus is to be operational, nor set forth a flow diagram as to the manner the device is to operate nor set forth guidance as to how prior art software should be/could be modified in order to enable the operation of the apparatus.

Note that the specification does not provide adequate guidance to teach how to load and unload PCR machine through a plurality of individual heat transfer stations and how to set up a program of a polymerase chain reaction. It would not be possible a skilled artisan, at the time of the subject application was filled, to perform a polymerase chain reaction without these guidances so as resort to undue experimentation.

Clearly, there will be a lot of unpredictable factors when the skilled artisan uses this apparatus and the skilled artisan will have no way to predict the experimental results. Such efforts constitute undue experimentation. The situation at hand is analogous to that in *Genentech v. Novo Nordisk A/S* 42 USPQ2d 1001. As set forth in the decision of the Court:

> " '[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation.' *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *see also Amgen Inc. v. Chugai Pharms. Co.*, 927 F. 2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed Cir. 1991); *In re Fisher*, 427 F. 2d 833, 166 USPQ 18, 24 (CCPA 1970) ('[T]he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.').
> "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. *See Brenner v. Manson*, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (starting, in context of the utility requirement, that 'a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.') Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention.
> "It is true . . . that a specification need not disclose what is well known in the art. *See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific starting material or any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skill in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research.

Note that these undue experimentations will include but not limit to: (1) redesign a reagent well with a size which fit the protocol of polymerase chain reaction; (2) set forth a software by which such an apparatus is to be operational; (3) how to loading and unloading of the machine and how to set up a program of a polymerase chain reaction. These undue experimentations would required several years to complete.

The Presence or Absence of Working Examples

The specification does not provide any working example.

The Nature of the Invention

The invention relates to an automated apparatus for performing a reagent protocol using polymerase chain reaction.

The State of the Prior Art

At the time of filling, an apparatus with water controlled high-speed thermal cycling system for polymerase chain reaction had been built (US Patent 5,508,197, filled on July 25, 1994). However, an apparatus for performing a reagent protocol using polymerase chain reaction with any size of reagent wells and without computer controlled thermal cycling system is a novel and an undeveloped are of the art.

The Relative Skill of Those in the Art

The relative skill of those in the art to which the invention most closely pertains is high, on par with those which hold a Ph.D. in biochemistry and computer biology.

The Predictability or Unpredictability of the Art

Note the specification does not: (1) enable the making of the apparatus for performing a reagent protocol using polymerase chain reaction with undefined size of reagent wells; (2) set forth any software by which such an apparatus is to be operational, nor set forth a flow diagram of commuter language as to the manner the device is to operate nor set forth guidance as to how prior art software should be/could be modified in order to enable the operation of the apparatus; and (3) provide adequate guidance to teach how to load and unload PCR machine through a plurality of individual heat transfer stations and how to set up a program of a polymerase chain reaction. Therefore, the predictability of the art is low. Further, the claimed invention relates directly to matters of physiology and chemistry which are inherently unpredictable and as such, require greater levels of enablement. As noted in *In re Fisher* 166 USPQ 18 (CCPA, 1970):

> In cases involving predictable factors, such as that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.

The Breadth of the Claims

The claims encompass an apparatus for performing a reagent protocol using polymerase chain reaction with any size of reagent wells and without computer controlled thermal cycling system. In view of the limited guidance and the acknowledged areas of difficulty, applicant is urged to consider narrowing the scope of the claims to that which attention has been directed.

Response to Arguments

A. Applicant indicated in page 3 of remarks that "The same descriptive was used in a $1,000,00.^{00}$ SBIR Grant that was filled with NIH. There haven't been any similar questions resulting from the filing ". Applicant's argument has been fully considered and has not been found pervasive toward the withdrawal of the rejection because SBIR Grant is not related to the examination of patent application.

B. At page 3, third and fourth paragraphs of remarks, applicant indicated that the examiner's rejection may base upon well known PCR protocol. The applicant's argument has been fully considered and has not been found pervasive toward the withdrawal of the rejection because the examiner's rejection has not based on well known PCR protocol.

C. Applicant asserted that :(1) the size and spacing of the reagent well do not need to be defined since well format in PCR apparatus is well known (first and second paragraphs in page 4 and third paragraph in page 7 of remarks); and (2) " the methods of process control are many and well established to anyone who would practice the art" (second paragraphs of page 5 of remarks).

Applicant's arguments have been fully considered and have not been found pervasive toward the withdrawal of the rejection. First, as suggested by applicant, the examiner did notice that the specification describes a well pattern of a 16×24 array on 4.5 mm centers with a well volume of 10 μl. However, claims 12-28 encompass an apparatus for performing a reagent protocol using polymerase chain reaction with any kind of well format (any size of reagent well). The specification does not provide adequate guidance for use of any kind of well format (any size of reagent well) in an apparatus for performing a reagent protocol using polymerase chain reaction. A agreement is seeming reached in that several different well formats could be used in different PCR apparatus (first paragraph of page 4 of remarks). Second, as suggested by applicant, the examiner did notice that the specification describes "the functions of each station and how they fit into the workflow diagram". The examiner also noticed that the specification (first paragraph of page 10) simply mentions some drive methods for PCR machine such as Geneva motions or walking beam motions or indexing motion using stepper motors or servomotor. However, the specification does not provide adequate guidances to show how to use these drive methods to operate PCR apparatus. For an automated PCR machine, the specification does not set forth any software by which such an apparatus is to be operational nor set forth a flow diagram for computer language as to the manner the device is to operate nor set forth guidance as to how prior art software should be/could be modified in order to enable the operation of the apparatus. Therefore, there will be a lot of unpredictable factors when the skilled artisan uses this apparatus and the skilled artisan will have no way to predict the experimental

results. Such efforts constitute undue experimentation. The situation at hand is analogous to that in *Genentech v. Novo Nordisk A/S* 42 USPQ2d 1001 (see above).

D. At page 5, third paragraph of remarks, applicant argues that "it is not the intent of this patent to teach PCR". Applicant's argument has been fully considered and has not been found pervasive toward the withdrawal of the rejection because the rejection did not base on PCR protocol.

E. At page 5, fourth paragraph of remarks, applicant argues that "as for loading and unloading the machine, it's not clear what additional information the examiner is requesting" since " the multiple well pipettors described in this application are in common use within the field of art" which "are described in detailed in US Patents Nos. 5,736,105 and 5,598,343". Applicant's argument has been fully considered and has not been found pervasive toward the withdrawal of the rejection because the examiner's rejection based on that the specification does not provide adequate guidance to teach how to load and unload of PCR machine through a plurality of individual heat transfer stations, not base on how to load and unload PCR sample as suggested by applicant in his remarks. It is also noted that US Patents applicant cited above have not been incorporated by reference into instant application.

F. At page 7, first paragraph of remarks, applicant argues that "The inventor has three years of work and development into the present invention. Specific working examples of the specific elements are the basis of the descriptive write-up". Applicant's argument has been fully considered and has not been found pervasive toward the withdrawal of the rejection because: (1)

the examiner's rejection did not based on the absence of working example; and (2) "specific working examples of the specific elements are" not " the basis of the descriptive write-up" because there is no working example in the specification.

G. The applicant's arguments on *Relative Skill of Those in the Art* and *The Predictability or Unpredictability of the Art* (page 7) have been fully considered and have not been found pervasive toward the withdrawal of the rejection because the examiner believed that designing a PCR machine need someone which hold a Ph.D. in biochemistry and computer biology and applicant is confusing the design and operation of PCR machine.

H. Page 7, last paragraphs bridging to page 8 , first paragraph of remarks, applicant argues that a computer controlled system is not required for this application. Applicant's argument has been fully considered and has not been found pervasive toward the withdrawal of the rejection. The examiner noticed that the most of PCR apparatus have a computer temperature controlled system. For example, an apparatus with water controlled high-speed thermal cycling system for polymerase chain reaction had been built with a computer control system (US Patent 5,508,197, filled on July 25, 1994).

9. Claims 12-28 remains rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

It is note that the specification does not provide an adequate written description of automated control (computer) means as a part of the apparatus for polymerase chain reaction since the specification does not have any description about how to use computer to control thermal cycling system and other element of the apparatus, and how to set up a program for polymerase chain reaction (see specification, pages 11 and 13). .

In view of the description in the specification, the subject application does not reasonably convey to one skilled in the art that applicant was in possession of products encompass in the claims at the time of the application was filled. Therefore, the written description requirement has not been satisfied.

In support of this position, attention is directed to the decision of *Vas-Cath inc. V. Mahurkar* 19 USPQ2d 1111 (CAFC, 1991):

> This court in *Wilder* (and the CCPA before it) clearly recognized, and we hereby reaffirm, that 35 U.S.C. 112, first paragraph, requires a "written description of the invention" which is separate and distinct from the enablement requirement. The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the "applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed*.

Response to Arguments

At page 7, last paragraph of remarks, applicant argues that: (1) no complex computer controlled system is required; (2) "any one involved in the art, not even skilled", based on " the logic of the system operation", can selected a computer controlled system. Applicant's argument

have been fully considered and have not been found pervasive toward the withdrawal of the rejection. Since the specification does not provide an adequate written description of automated control (computer) means as a part of PCR apparatus, the subject application does not reasonably convey to one skilled in the art that applicant was in possession of products encompass in the claims at the time of the application was filled. Therefore, the written description requirement has not been satisfied. The situation at hand is analogous to the decision of *Vas-Cath inc. V. Mahurkar* 19 USPQ2d 1111 (CAFC, 1991) (see above).

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 12 and 26 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

12. The term "specific time controlled period" in claim 26 is a relative term which renders the claim indefinite. The term "specific time controlled period" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Response to Arguments

The applicant's argument has been fully considered and has not been found pervasive toward the withdrawal of the rejection because applicant appears to be in agreement in that " the term "specific time controlled period" is not defined by this invention".

13. Claims 12-28 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: a computer temperature controlled system in the apparatus for polymerase chain reaction.

Response to Arguments

At page 9, first paragraph of remarks, applicant argues that" the omission of a computer temperature controlled system" is only in the Examiner's view of how he would control the system. It is not an omission on the part of this application". Applicant's argument has been fully considered and has not been found pervasive toward the withdrawal of the rejection. The examiner noticed that the most of PCR apparatus has a computer temperature controlled system. For example, an apparatus with water controlled high-speed thermal cycling system for polymerase chain reaction had been built with a computer control system (US Patent 5,508,197, filled on July 25, 1994). Applicant has no evidence to show that PCR apparatus in this application has been made without a computer control system.

At page 9, second paragraph of remarks, applicant argues that "the Hansen et al. Patent cited by the examiner appears to have about the same degree of disclosure as the present application". Applicant's argument has been fully considered and has not been found pervasive toward the withdrawal of the rejection because each application is considered on an individual basis.

Conclusion

14. Rejections found in the prior office action yet not restated herein above have been withdrawn.

15. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

16. No Claim is allowed.

17. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (703) 305-1270. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

Frank Lu
September 25, 2000

B. L. Sisson

BRADLEY L. SISSON
PRIMARY EXAMINER
GROUP 1800

10/2/00